CONSENT TO ACT AS RESEARCH SUBJECT (CORONARY ARTERY DISEASE SUBJECT) "Evaluation of New Instrument for the Assessment of Vascular Function" (RMP #68)

You are being invited to participate as a subject in a research project headed by Dr. Thomas F. Budinger M.D., Ph.D. at the University of California, Berkeley, University of California, San Francisco and Lawrence Berkeley National Laboratory (LBNL), and by Jonathan S. Maltz, Ph.D. at LBNL. The purpose of this project is to compare how well two different devices measure blood flow in the arteries of the arm. The final goal is to produce a small, low-cost device that could be used as part of a routine medical check-up. A device like this could help doctors to find diseases of the arteries at an early stage. The study will be conducted at the University of California's Lawrence Berkeley National Laboratory (LBNL), in the Department of Functional Imaging.

You are being asked to participate in this study because you have coronary artery disease. You are being asked to volunteer to participate in 3 studies, including today. You may be asked to come back for up to 12 more study days in future. On each study day you will complete a screening form, and then undergo up to 3 of the procedures listed below. You will be given 30 minutes to rest between procedures. Completing a study day will take as long as 3 hours 45 minutes. Study days will be arranged at your convenience.

At the end of the study, we may draw 33ml of blood (about 2 tablespoons). We do this to measure your levels of cholesterol and other substances that affect the response of your blood vessels.

We will ask your permission to allow us to access your medical records to obtain information relevant to this study.

1 Procedures

On each study day, you will first fill out a screening form to see of you are eligible to participate in the experimental procedures described below.

1.1 Procedure A (Tapping device with tightened blood pressure cuff)

1. A blood pressure cuff will be applied to your upper left forearm. A blood pressure reading will be taken, but the cuff will not be removed.
2. While seated comfortably, you will place your arm onto a metal platform at chest height. Straps may be used to hold the arm in one place comfortably.
3. A mechanical device will gently tap your arm at the wrist throughout the procedure.

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4. A gel will be applied to your wrist or forearm and a device to measure blood flow using sound waves will be positioned over this area so that it is directly over an artery in the forearm. The device is known as a Doppler stethoscope.

5. An initial measurement will be made before the blood pressure cuff is tightened.

6. The blood pressure cuff on your upper arm will be tightened above 200 mmHg for 5 to 6 minutes. During this time more measurements will be taken. The pressure is similar to that used in making blood pressure measurements but the time it is applied is much longer. There will be some discomforts such as a squeezing sensation in the arm and tingling in the hand.

7. One minute after the cuff is loosened more measurements will be made for another ten minutes. Some of these measurements may involve a brief retightening of the cuff for no longer than 60 seconds at a time.

The amount of time to complete this procedure is approximately 32 minutes.

1.2 Procedure B (Scanning device with tightened blood pressure cuff)

1. Your arm will be placed in an arm holder and secured into place.

2. EKG electrodes will be placed on your arms and chest or possibly on a single finger.

3. Another blood pressure measurement will be taken and the cuff will not be removed.

4. A series of measurements will be taken with an ultrasound probe which may take up to 10 minutes.

5. The blood pressure cuff on your upper arm will be tightened above 200 mmHg for 5 to 6 minutes. During this time more measurements will be taken.

6. One minute after the cuff is loosened more measurements will be made for another ten minutes. Some of these measurements may involve the brief retightening of the cuff for no longer than 60 seconds at a time. The amount of time to complete this procedure is approximately 35 minutes.

   The investigators may choose to reverse the order in which these devices are tested. For example, You may have your first set of measurements taken with Device B followed 40 minutes later by Device A. On your first visit, if you are chosen to participate in the Device B procedure first, an additional measurement will be made forty minutes after the cuff release. This measurement will not involve any tightening of the cuff.

The amount of time to complete this procedure is approximately 35 minutes.

1.3 Procedure C (Tapping device with nitroglycerin tablet or inhaled spray)

1. A blood pressure reading will be taken.

2. While seated comfortably, you will place your arm onto a metal platform at chest height. Straps may be used to hold the arm in one place comfortably.

3. A mechanical device will gently tap your arm at the wrist throughout the procedure.

4. A gel will be applied to your wrist or forearm and a device to measure blood flow using sound waves will be positioned over this area so that it is directly over an artery in the forearm. The device is known as a Doppler stethoscope.

5. You will be given a nitroglycerin tablet to place under your tongue (this tablet will dissolve and should not be chewed), or you will be asked to inhale albuterol with an inhaler.

6. Measurements will continue for up to fifteen minutes. You will simply need to keep your arm still and remain seated during this time.

The amount of time to complete this procedure is approximately 42 minutes.

1.4 Procedure D (Scanning device with nitroglycerin tablet or inhaled spray)

1. Your arm will be placed in an arm holder and secured into place.

2. EKG electrodes will be placed on your arms and chest or possibly on a single finger.

3. Another blood pressure measurement will be taken and the cuff will not be removed.

4. A series of measurements will be taken with this second device which may take up to 10 minutes.

5. You will be given a nitroglycerin tablet to place under your tongue (this tablet will dissolve and should not be chewed), or you will be asked to inhale albuterol with an inhaler.

6. Measurements will continue for up to fifteen minutes. You will simply need to keep your arm still and remain seated or lying down during this time.

   The amount of time to complete this procedure is approximately 36 minutes.

The total amount of time you will spend being involved in experiments on one study day ranges from 1.5 to 3 hours, depending on which of the following combinations of procedures will be carried out on one day:

1. A (left arm), A (right arm) (1 hour 34 min, 2 occlusions)

2. B (left arm), B (right arm) (1 hour 40 min, 2 occlusions)

3. A, B, C (2 hours 47 min, 2 occlusions)

4. A, B, D (2 hours 41 min, 2 occlusions)

5. B, A, C (2 hours 47 min, 2 occlusions)

6. A, B (1 hour 37 min, 2 occlusions)

7. B, A (1 hour 37 min, 2 occlusions)

8. A, C (1 hour 34 min, 1 occlusion)

9. C, A (1 hour 34 min, 1 occlusion)
10. B, C (1 hour 42 mi, 1 occlusionn)
11. C, B (1 hour 42 min, 1 occlusion)
12. C, D (1 hour 48 min)
13. D, C (1 hour 48 min)

If you are a woman of child-bearing age, we will administer a pregancy test to see if you may participate in any of the experiments that the involve administration of a drug (Procedures C and D).

2 Exclusions

If any of the following apply to you, you may not participate in this study.

1. If you have severe damage to the arteries in your arm.
2. If your arm is severely bruised on the day of the study.
3. If you have high blood pressure (for example 170/100 mmHg), or low blood pressure (lower than 90/60).
4. If you have vascular implants (such as those used in dialysis).
5. If, in the last week, you have had blood samples taken from an arm that will be experimented upon.
6. If you have severe leg pain due to problems with the arteries and veins in your legs.
7. If you have had blood clots in the past.
8. If you have had any needles inserted into your arm within the last two days.
9. If you have taken Viagra (sildenafil), Levitra (vardenafil), Cialis (tadenafil) or similar medications used to treat erectile dysfunction within the last 24 hours, or plan to take one of these medications today.
10. If you are pregnant you will be excluded from Procedures C and D.
11. If you have known allergies to albuterol, or have taken medication for asthma, heart disease or depression, such as atenolol (Tenormin); carteolol (Cartrol); labetalol (Normodyne, Trandate); metoprolol (Lopressor); nadolol (Corgard); phenelzine (Nardil); propranolol (Inderal); sotalol (Betapace); theophylline (Theo-Dur); timolol (Blocadren); tranylcypromine (Parnate), and trycyclic antidepressants such as Elavil and you are scheduled to undergo Procedure D.
12. If you have known allergies to nitroglycerin, have anemia, glaucoma, or have taken medication such as calcium channel blockers like amlodipine (Norvasc), diltiazem (Cardizem), felodipine (Plendil), isradipine (DynaCirc), nifedipine (Procardia), and verapamil (Calan, Isoptin); dihydroergotamine (D.H.E. 45) and you are scheduled to undergo Procedure C.

13. If you are taking prescription blood thinners.

14. If you have migraine headaches; cardiac arrythmias; congestive heart failure. If you have had a heart attack within the last 12 months. If you have unstable coronary artery disease.

15. If you have a known allergy to electrode paste.

16. If you are scheduled for a study involving nitroglycerin and have taken this drug as a tablet, spray, patch or gel in the past 8 hours, your study will be deferred by at least 4 to 8 hours depending on the type of nitroglycerin you have taken.

3 RISKS/DISCOMFORTS

This procedure has the following possible risks and discomforts:

1. The blood draws involve the pain of a needle insertion and there can be a bruise following the blood draws. In rare cases, an infection may occur.

2. There may be some slight forearm bruising to the skin in the area where pressure from the device used in Procedure A and C is applied over your artery.

3. There is usually discomfort or a tingling sensation from the tightened blood pressure cuff (Procedures A and B). This discomfort disappears rapidly after the cuff is released.You may ask to have the cuff and restraints removed at any time if it becomes too uncomfortable.

4. The electrode paste may irritate your skin.

5. In Procedures C and D, the nitroglycerin tablet may cause you to experience dizziness, lightheadedness, fainting when sitting or standing, headache and a tingling or burning sensation in the mouth, and flushing of the face and neck. You should sit up or stand up slowly to lower the risk of falling or fainting. It is dangerous to take nitroglycerin in combination with drugs such as Viagra (sildenafil citrate) used to treat erectile dysfunction. Taking nitroglycerin is a commonplace treatment for chronic angina, the chest pain of heart disease. It works by relaxing the blood vessels to the heart, so the blood flow and oxygen supply to the heart is increased. The regular dose is 0.4 mg.

6. In Procedures C and D, you may be asked to inhale albuterol. Albuterol, when given repeatedly for relief of respiratory symptoms, may have short term side effects including dizziness or drowsiness, anxiety, headache, fast heart beat, increased blood pressure, upset stomach, cough, or difficulty in falling or staying asleep. In this application only one administration (2 inhalations) is involved and no side effects are expected. In the event of symptoms of anxiety, increased heart rate or dizziness, you will be advised the symptoms will disappear in about 15 minutes. You will be accompanied by a researcher during the period of symptoms.

7. In Procedures C and D, nitroglycerin and/or albuterol may cause an allergic reaction, although this is very unlikely to occur.

8. In Procedures C and D, nitroglycerin and albuterol may pose additional risks because you have coronary artery disease. In the event of rapid heart rate for more than a few minutes, or dizziness or shortness of breath for more than four minutes, you will be monitored continuously by blood pressure measurements and have a doctor in attendance who will evaluate your EKG.

The maxmium total length of the study today will be less than two hours.

4 Compensation for injury

If you are injured as a result of taking part in this study, medical care and treatment will be available to you as a participating subject. The costs of this care may be covered by the University of California depending on a number of factors. The University does not normally provide any other compensation for injury. If you have any questions regarding this assurance, you may consult or call the Berkeley Lab Human Subjects Committee, MS 26-143, 1 Cyclotron Road, Berkeley, CA 94720 (510) 486-5507 or the Committee for the Protection of Human Subjects, 101 Wheeler Hall, University of California, Berkeley, 94720-1340, (510) 642-746l.

5 Benefits

There are no direct benefits to you as a subject in this research. These devices may benefit future patients, through the development of a routine method of early diagnosis of arterial disease.

6 Storage of samples and data

Once you are enrolled, we intend to retain and use your data for our study, even if you later drop out or are excluded from our study. Your records will be kept as confidential as possible within the law. Individual identities will not be used in any reports or publications resulting from this study. Storage of data will be at the Lawrence Berkeley National Laboratory in the Department of Nuclear Medicine and Functional Imaging. We will discard any blood samples not sent for analysis. We will not share any samples with collaborating institutions. We will not share any data with collaborating institutions that reveals your identity.

7 Financial compensation

You will receive $75 for each day that you participate in this study. You will be reimbursed for travel expenses to and from the laboratory on each day.

8 Questions

Any questions you have about your right as a research subject will be answered by the Berkeley Lab Human Subjects Committee at (510) 486-5507 or the University of California at Berkeley Committee for the Protection of Human Subjects (510) 642-7461.

9 Participation in research is voluntary

You have the right to not take part in this study or to stop taking part at any time. You will be given a copy of this consent form and the Experimental Subject's Bill of Rights to keep.